```
  1 GGCACGAGGAGATCTAGGTTCAAATTAATGTTGCCCCTAGTGGTAAAGGACAGAGACCCTCAGACTGATGAAATGCGCTCAGAATTACTT
 91 AGACAAAGCGGATATTTGCCACTCTCTTCCCCTTTTCCTGTGTTTTTGTAGTGAAGAGACCTGAAAGAAAAAAGTAGGGAGAACATAATG
                                                  *  *

181 AGAACAAATACGGTAATCTCTTCATTTGCTAGTTCAAGTGCTGGACTTGGGACTTAGGAGGGGCAATGGAGCCGCTTAGTGCCTACATCT
                                                        *

271 GACTTGGACTGAAATATAGGTGAGAGACAAGATTGTCTCATATCCGGGGAAATCATAACCTATGACTAGGACGGGAAGAGGAAGCACTGC
          *                                                    *

361 CTTTACTTCAGTGGGAATCTCGGCCTCAGCCTGCAAGCCAAGTGTTCACAGTGAGAAAAGCAAGAGAATAAGCTAATACTCCTGTCCTGA
                                                        *                                   *

451 ACAAGGCAGCGGCTCCTTGGTAAAGCTACTCCTTGATCGATCCTTTGCACCGGATTGTTCAAAGTGGACCCCAGGGGAGAAGTCGGAGCA
                                          *

541 AAGAACTTACCACCAAGCAGTCCAAGAGGCCCAGAAGCAAACCTGGAGGTGAGACCCAAAGAAAGCTGGAACCATGCTGACTTTGTACAC
                                                L  E  V  R  P  K  E  S  W  N  H  A  D  F  V  H     16

631 TGTGAGGACACAGAGTCTGTTCCTGGAAAGCCCAGTGTCAACGCAGATGAGGAAGTCGGAGGTCCcCAAATCTGCCGTGTATGTGGGGAC
    C  E  D  T  E  S  V  P  G  K  P  S  V  N  A  D  E  E  V  G  G  P  Q  I  C  R  V  C  G  D     46

721 AAGGCCACTGGCTATCACTTCAATGTCATGACATGTGAAGGATGCAAGGGCtTTTTCAGGAGGGCCATGAAACGCAACGCCCGGCTGAGG
    K  A  T  G  Y  H  F  N  V  M  T  C  E  G  C  K  G  F  F  R  R  A  M  K  R  N  A  R  L  R     76

811 TGCCCcTTCCGGAAGGGCGCCTGCGAGATCACCCGGAAGACCCGGCGACAGTGCCAGGCCTGCCGCCTGCGCAAGTGCCTGGAGAGCGGC
    C  P  F  R  K  G  A  C  E  I  T  R  K  T  R  R  Q  C  Q  A  C  R  L  R  K  C  L  E  S  G    106

901 ATGAAGAAGGAGATGATCATGTCCGACGAGGCCGTGGAGGAGAGGCGGGCCTTGATCAAGCGGAAGAAAAGTGAACGGACAGGGACTCAG
    M  K  K  E  M  I  M  S  D  E  A  V  E  E  R  R  A  L  I  K  R  K  K  S  E  R  T  G  T  Q    136
```

FIGURE 1A-1

```
991 CCACTGGGAGTGCAGGGGCTGACAGAGGAGCAGCGGATGATGATCAGGGAGCTGATGGACGCTCAGATGAAAACCTTTGACACTACCTTC
    P  L  G  V  Q  G  L  T  E  E  Q  R  M  M  I  R  E  L  M  D  A  Q  M  K  T  F  D  T  T  F    166

1081 TCCCATTTCAAGAATTTCCGGCTGCCAGGGGTGCTTAGCAGTGGCTGCGAGTTGCCAGAGCCTCTGCAGGCCCCATCGAGGGAAGAAGCT
     S  H  F  K  N  F  R  L  P  G  V  L  S  S  G  C  E  L  P  E  P  L  Q  A  P  S  R  E  E  A    196

1171 GCCAAGTGGAGCCAGGTCCGGAAAGATCTGTGCTCTTTGAAGGTCTCTCTGCAAGCTGCGGGGGGGAGGATGGCAGTGTCTGGAACTACAA
     A  K  W  S  Q  V  R  K  D  L  C  S  L  K  V  S  L  Q  A  A  G  G  G  W  Q  C  L  E  L  Q    226

1261 ACNCCCAGCCGACAGTGGCGGAAAGAGATCTTCTCCCTGCTGCCCCACATGGCTGACATGTCAACCTACATGTTCAAAGGCATCATCAGC
     T  P  S  R  Q  W  R  K  E  I  F  S  L  L  P  H  M  A  D  M  S  T  Y  M  F  K  G  I  I  S    256

1351 TTTGCCAAAGTCATCTCCTACTTCAGGGACTTGCCCATCGAGGACCAGATCTCCCTGCTGAAGGGGGCCGCTTTCGAGCTGTGTCAACTG
     F  A  K  V  I  S  Y  F  R  D  L  P  I  E  D  Q  I  S  L  L  K  G  A  A  F  E  L  C  Q  L    286

1441 AGATTCAACACAGTGTTCAACGCGGAGACTGGAACCTGGGAGTGTGGCCGGCTGTCCTACTGCTTGGAAGACACTGCAGGTGGCTTCCAG
     R  F  N  T  V  F  N  A  E  T  G  T  W  E  C  G  R  L  S  Y  C  L  E  D  T  A  G  G  F  Q    316

1531 CAACTTCTACTGGAGCCCATGCTGAAATTCCACTACATGCTGAAGAAGCTGCAGCTGCATGAGGAGGAGTATGTGCTGATGCAGGCCATC
     Q  L  L  L  E  P  M  L  K  F  H  Y  M  L  K  K  L  Q  L  H  E  E  E  Y  V  L  M  Q  A  I    346

1621 TCCCTCTTCTCCCCAGACCGCCCAGGTGTGCTGCAGCACCGCGTGGTGGACCAGCTGCAGGAGCAATTCGCCATTACTCTGAAGTCCTAC
     S  L  F  S  P  D  R  P  G  V  L  Q  H  R  V  V  D  Q  L  Q  E  Q  F  A  I  T  L  K  S  Y    376

1711 ATTGAATGCAATCGGCCCCAGCCTGCTCATAGGTTCTTGTTCCTGAAGATCATGGCTATGCTCACCGAGCTCCGCAGCATCAATGCTCAG
     I  E  C  N  R  P  Q  P  A  H  R  F  L  F  L  K  I  M  A  M  L  T  E  L  R  S  I  N  A  Q    406

1801 CACACCCAGCGGCTGCTGCGCATCCAGGACATACACCCCTTTGCTACGCCCCTCATGCAGGAGTTGTTCGGCATCACAGGTAGCTGAGCG
     H  T  Q  R  L  L  R  I  Q  D  I  H  P  F  A  T  P  L  M  Q  E  L  F  G  I  T  G  S  *      434

1891 GCTGCCTTGGGTGACACCTTCGAGAGGCAGCCAGACCCAGAGCCCTCTGAGCCGGCACTCCCGGGCCAAGACAGATGGACACTGCCAAGA
1981 GCCGACAATGCCCTGCTGGCCTGTCTCCCTAGGGAATTCCTGCTATGACAGCTGGCTAGCATTCCTCAGGAAGGACATGGGGTGCCCC  2068
```

FIGURE 1A-2

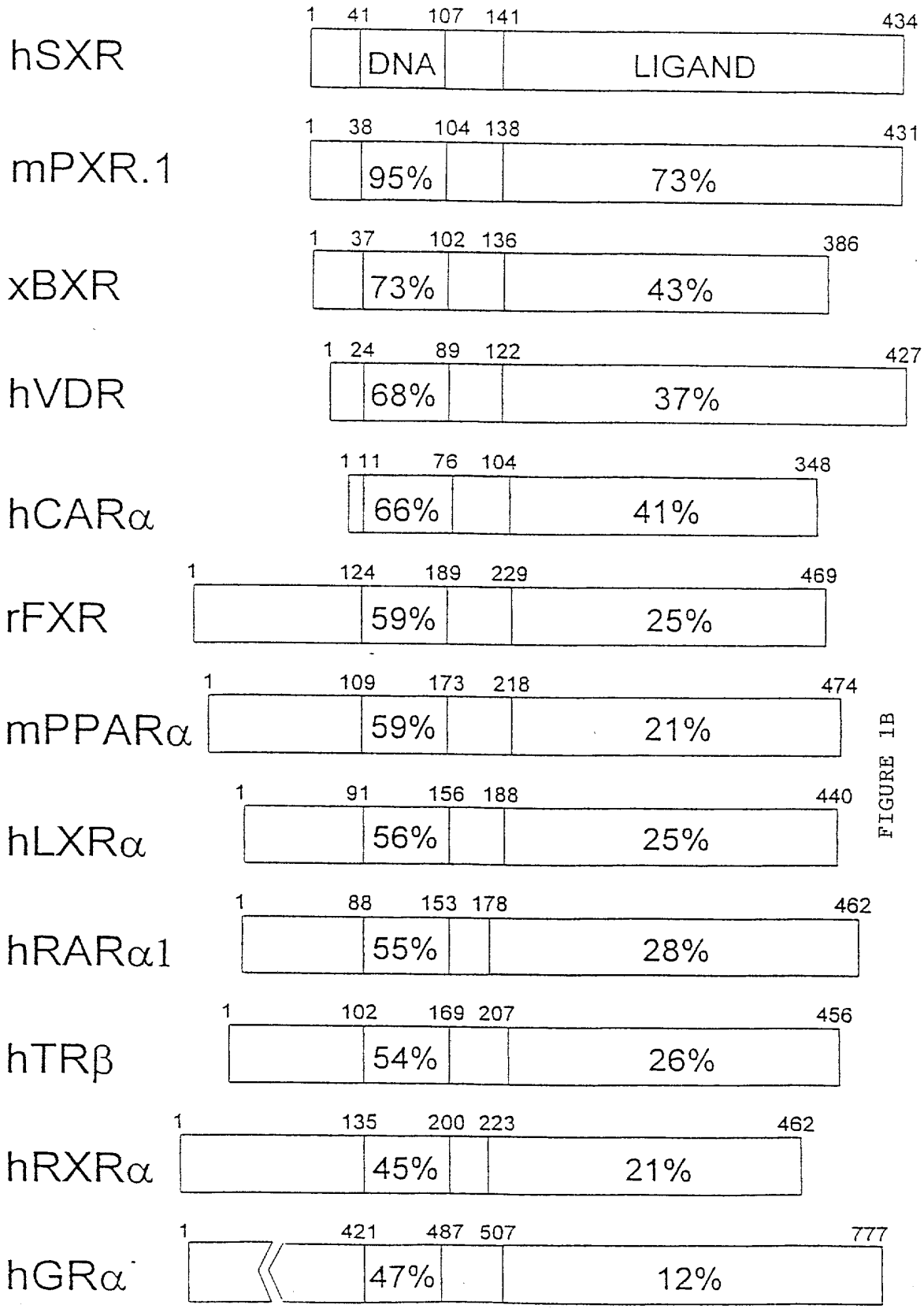
hSXR
1 41 107 141 434
DNA
LIGAND
mPXR.1
1 38 104 138 431
95%
73%
xBXR
1 37 102 136 386
73%
43%
hVDR
1 24 89 122 427
68%
37%
hCARα
1 11 76 104 348
66%
41%
rFXR
1 124 189 229 469
59%
25%
mPPARα
1 109 173 218 474
59%
21%
hLXRα
1 91 156 188 440
56%
25%
hRARα1
1 88 153 178 462
55%
28%
hTRβ
1 102 169 207 456
54%
26%
hRXRα
1 135 200 223 462
45%
21%
hGRα
1 421 487 507 777
47%
12%

FIGURE 1B

20020220 SSST3001

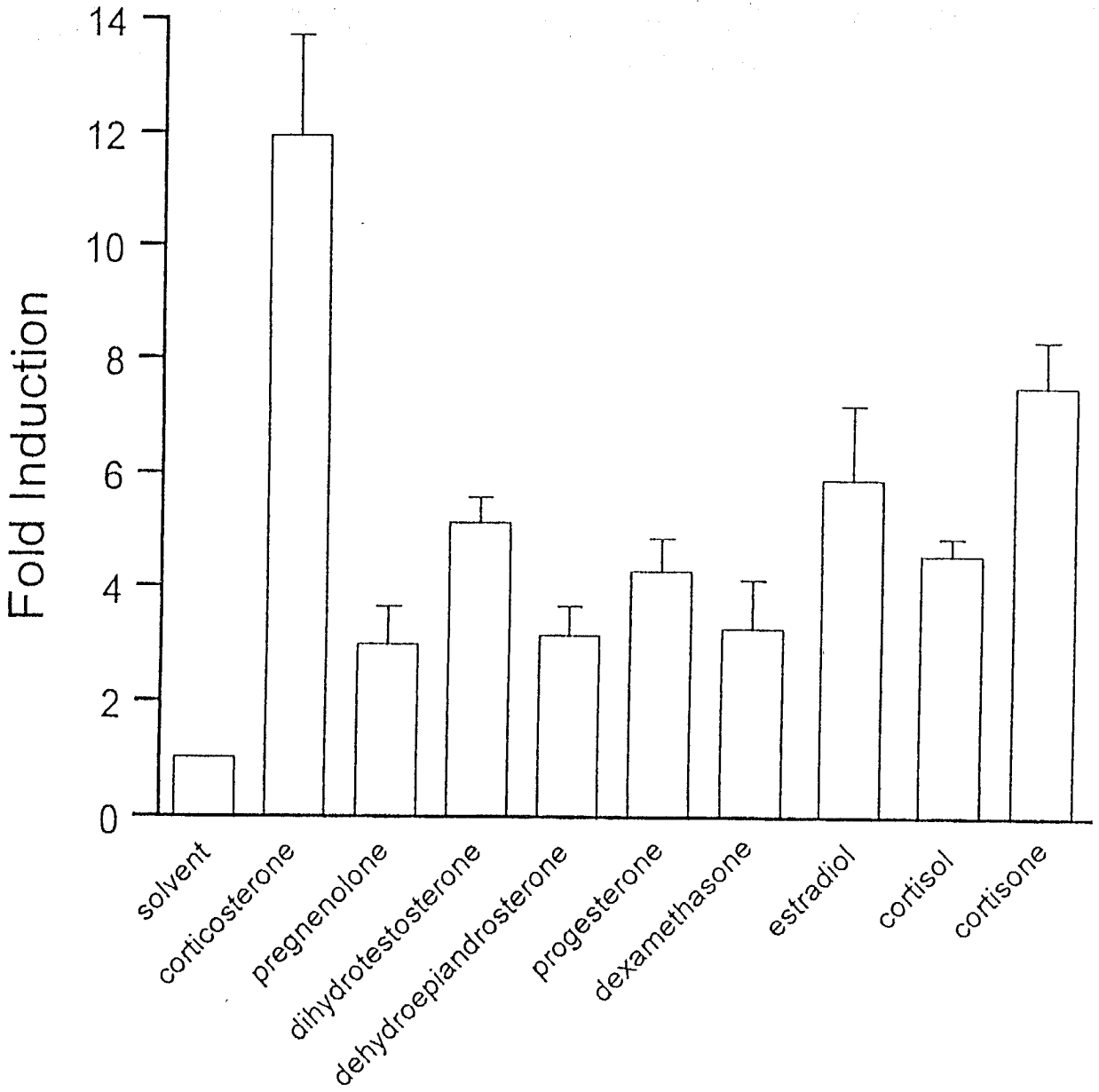

Figure 2

20020820 SSSTB001

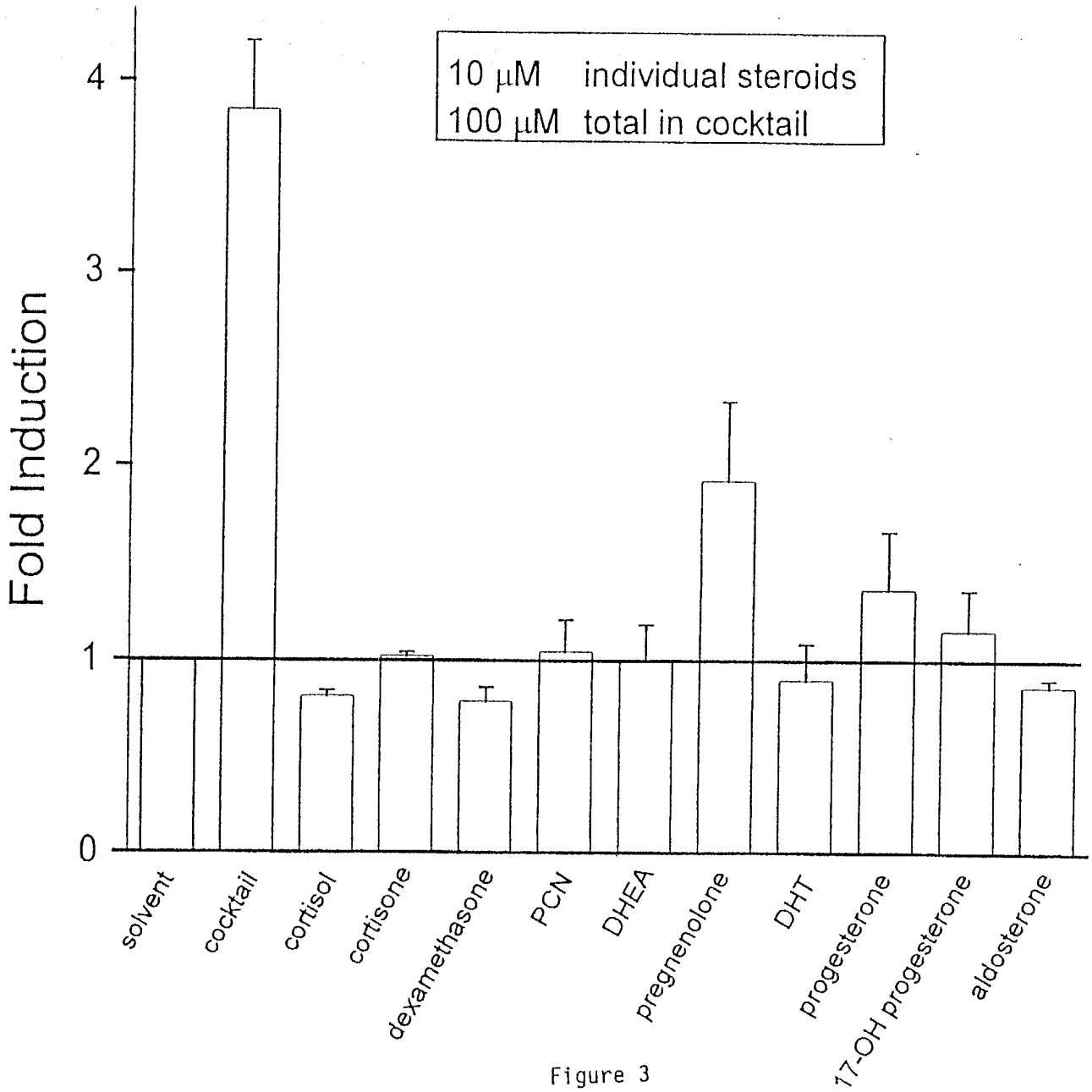

Figure 3

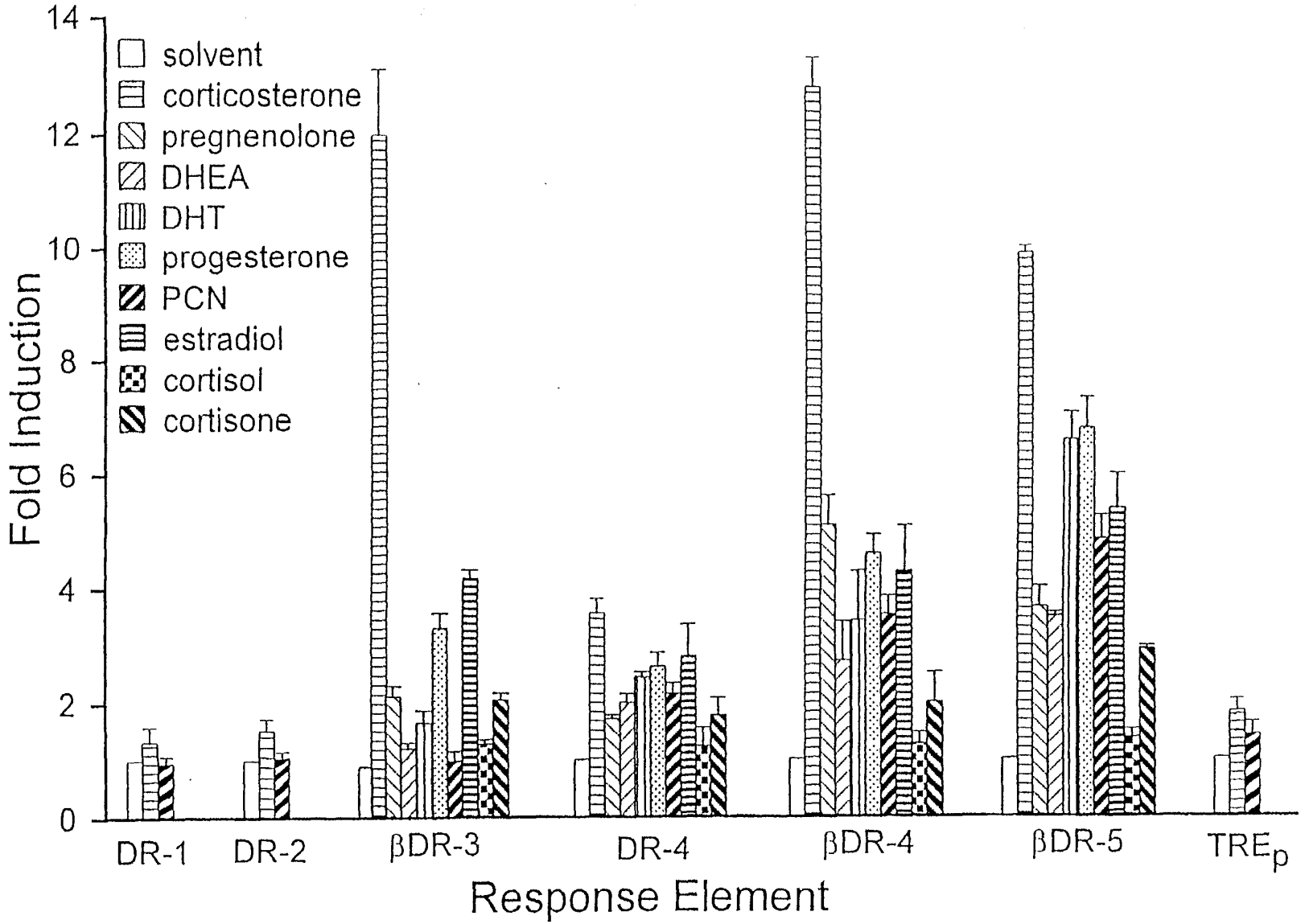
14
12
10
8
6
4
2
0
Fold Induction
solvent
corticosterone
pregnenolone
DHEA
DHT
progesterone
PCN
estradiol
cortisol
cortisone
DR-1
DR-2
βDR-3
DR-4
βDR-4
βDR-5
TREp
Response Element

Figure 4

Applicant's Exhibit

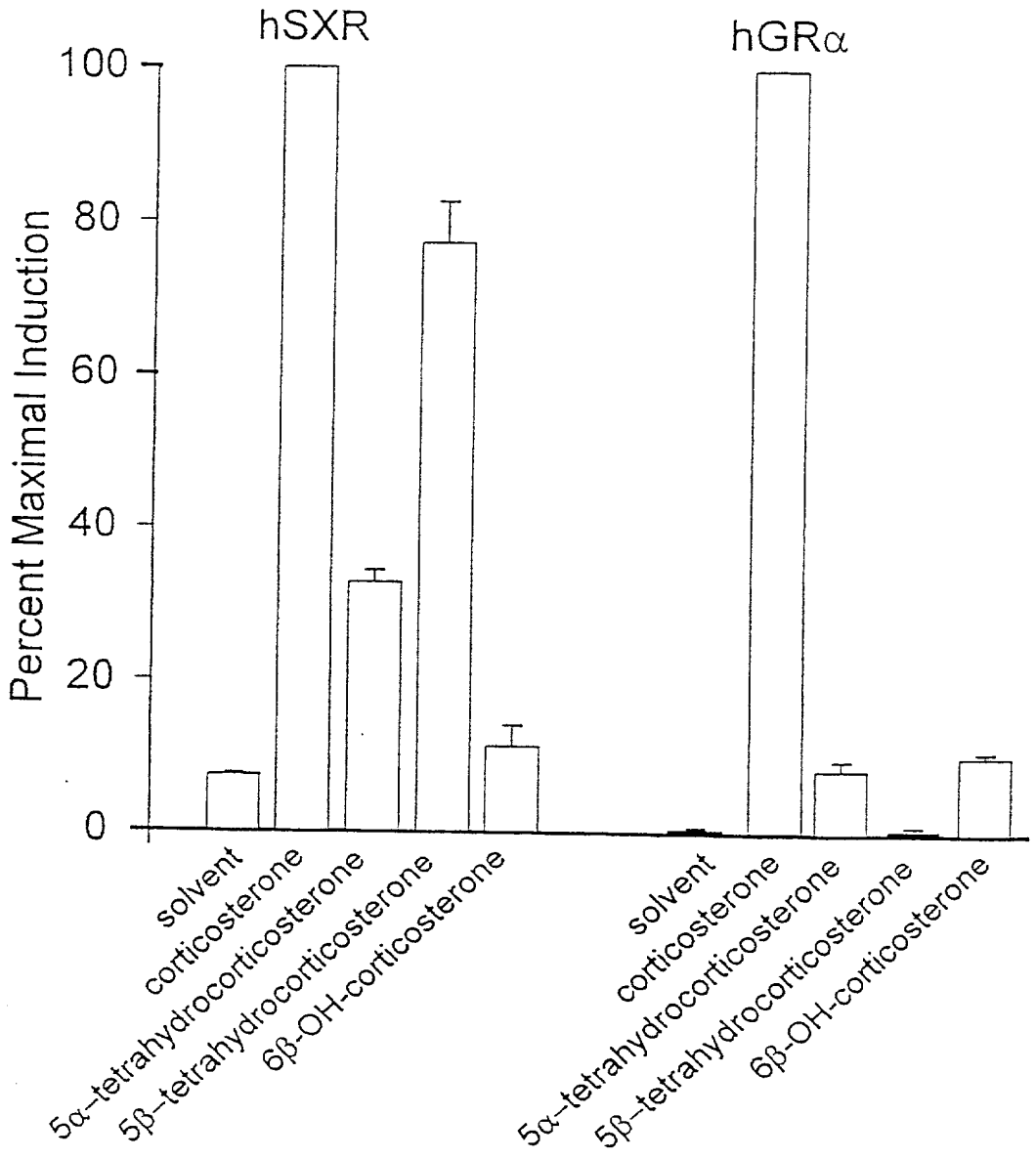

Figure 5.

300220 "SSSTBOOT

DR-3

rCYP3A1	tagac **AGTTCA** tga **AGTTCA** tctac
rCYP3A2	taagc **AGTTCA** taa **AGTTCA** tctac
rUGT1A6	actgt **AGTTCA** taa **AGTTCA** catgg

DR-4

rbCYP2C1	caatc **AGTTCA** acag **GGTTCA** ccaat
rP450R	cac **AGGTGA** gctg **AGGCCA** gcagc **AGGTCG** aaa

DR-5

rCYP2A1	gtgca **GGTTCA** actgg **AGGTCA** acatg
rCYP2A2	gtgct **GGTTCA** actgg **AGGTCA** gtatg
rCYP2C6	agtct **AGTTCA** gtggg **GGTTCA** gtctt
hCYP2E1	gagat **GGTTCA** aggaa **GGGTCA** ttaac

Figure 6A

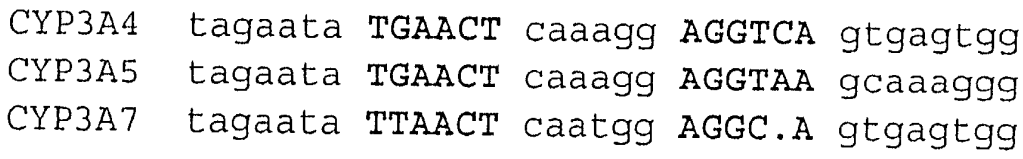
CYP3A4 tagaata TGAACT caaagg AGGTCA gtgagtgg
CYP3A5 tagaata TGAACT caaagg AGGTAA gcaaaggg
CYP3A7 tagaata TTAACT caatgg AGGC.A gtgagtgg

Figure 6B

Applicant's Exhibit

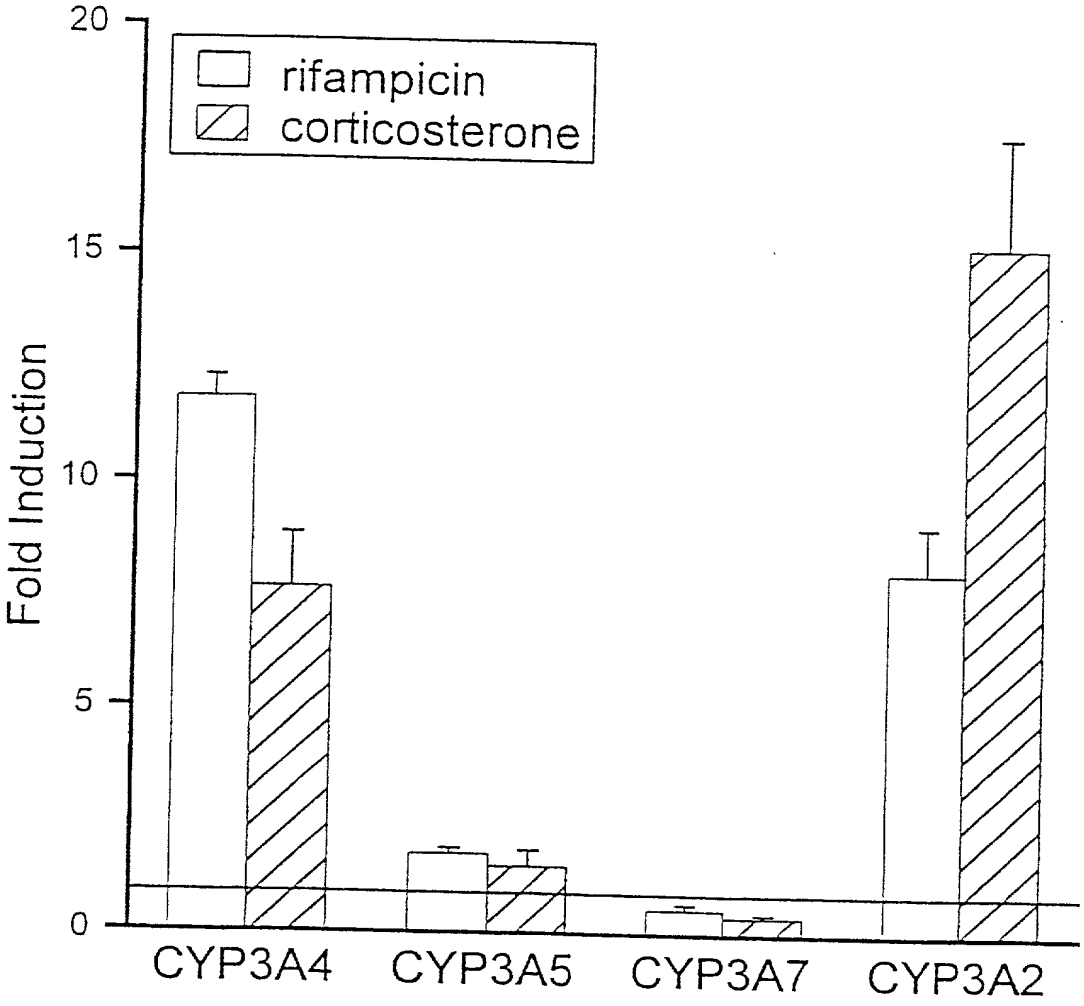

Figure 6C

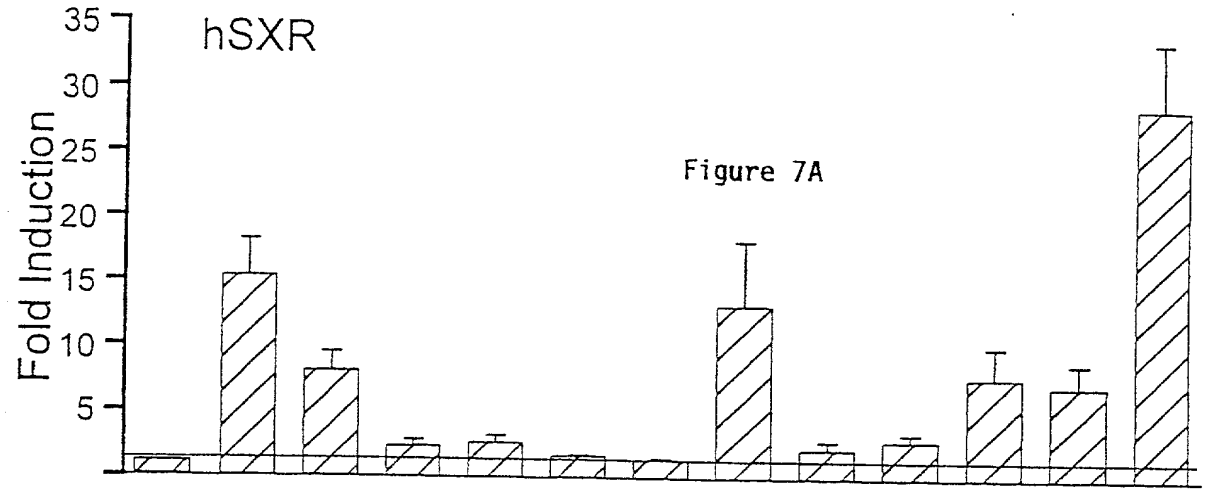

Figure 7A

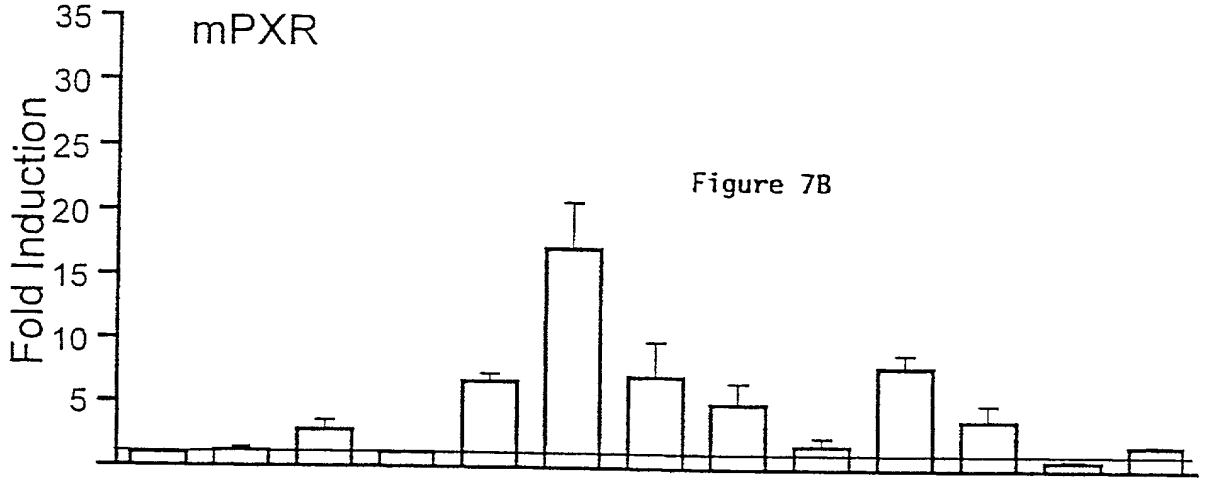

Figure 7B

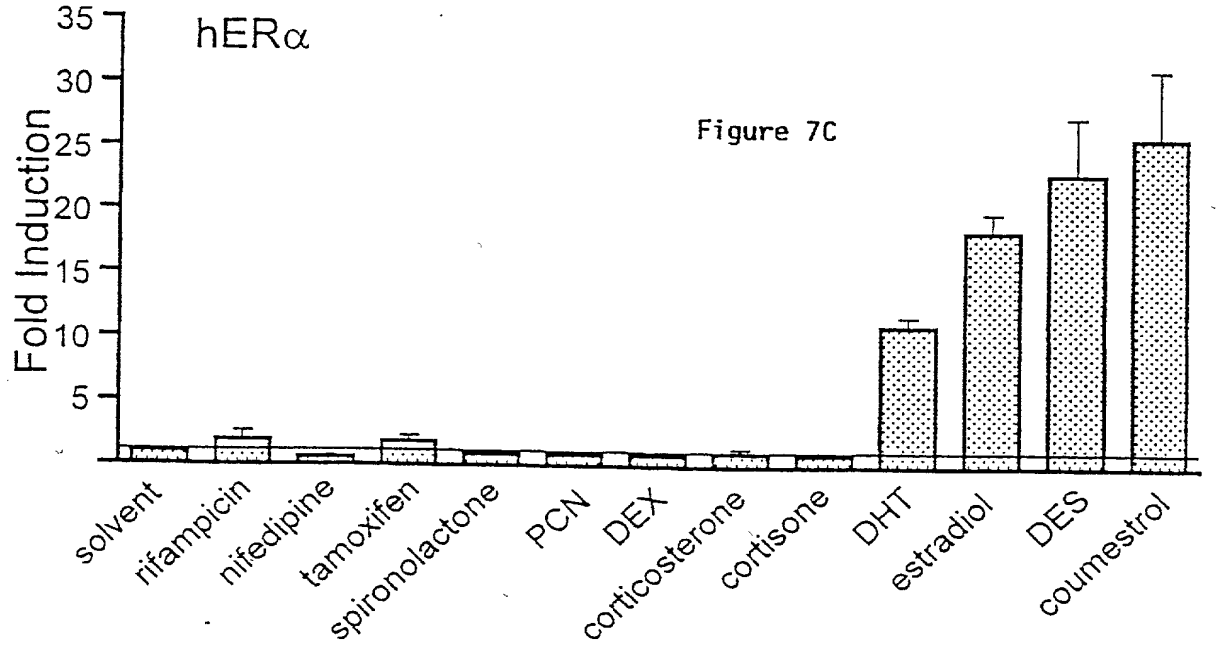

Figure 7C

20020155.020202

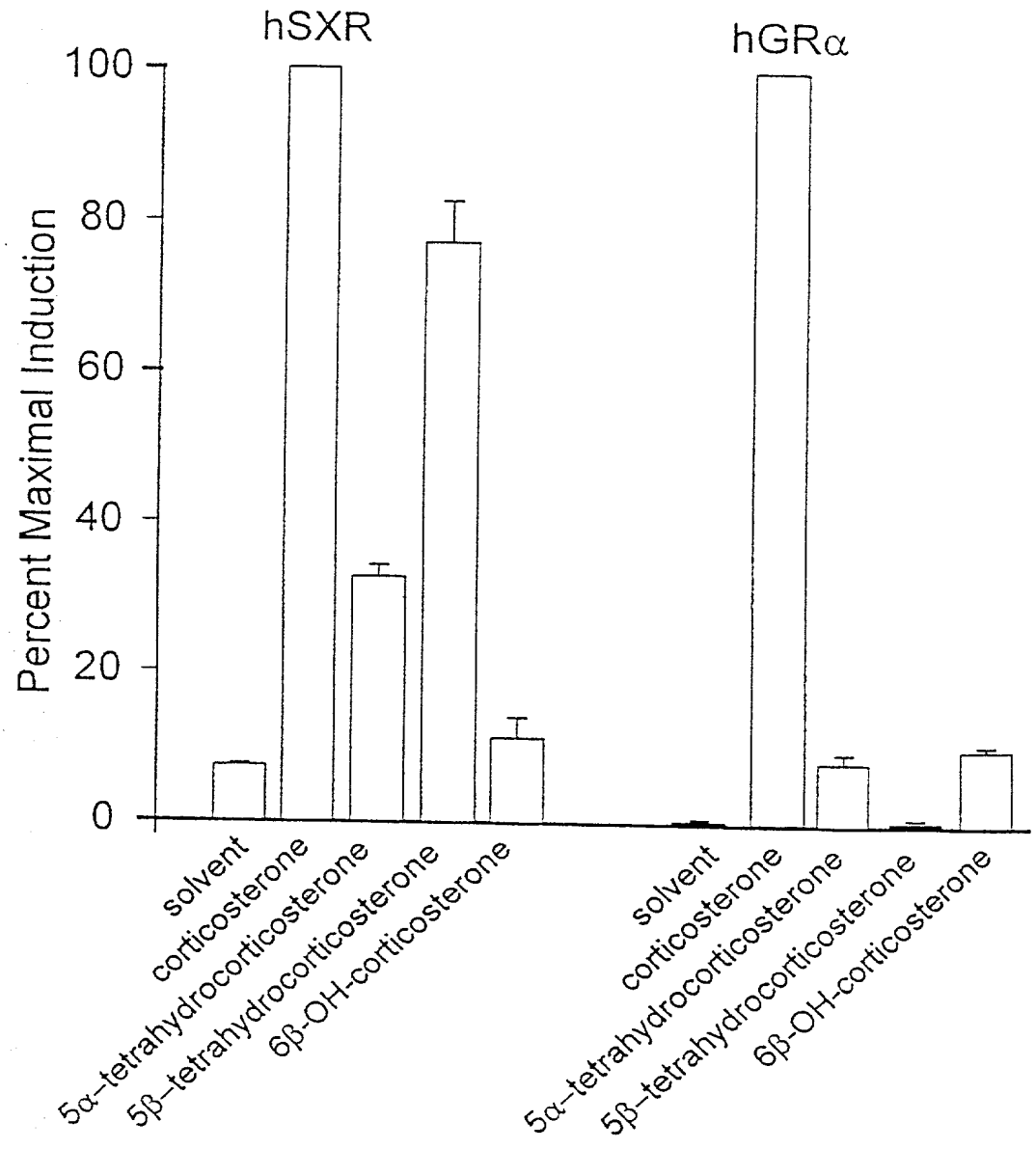

Figure 7D

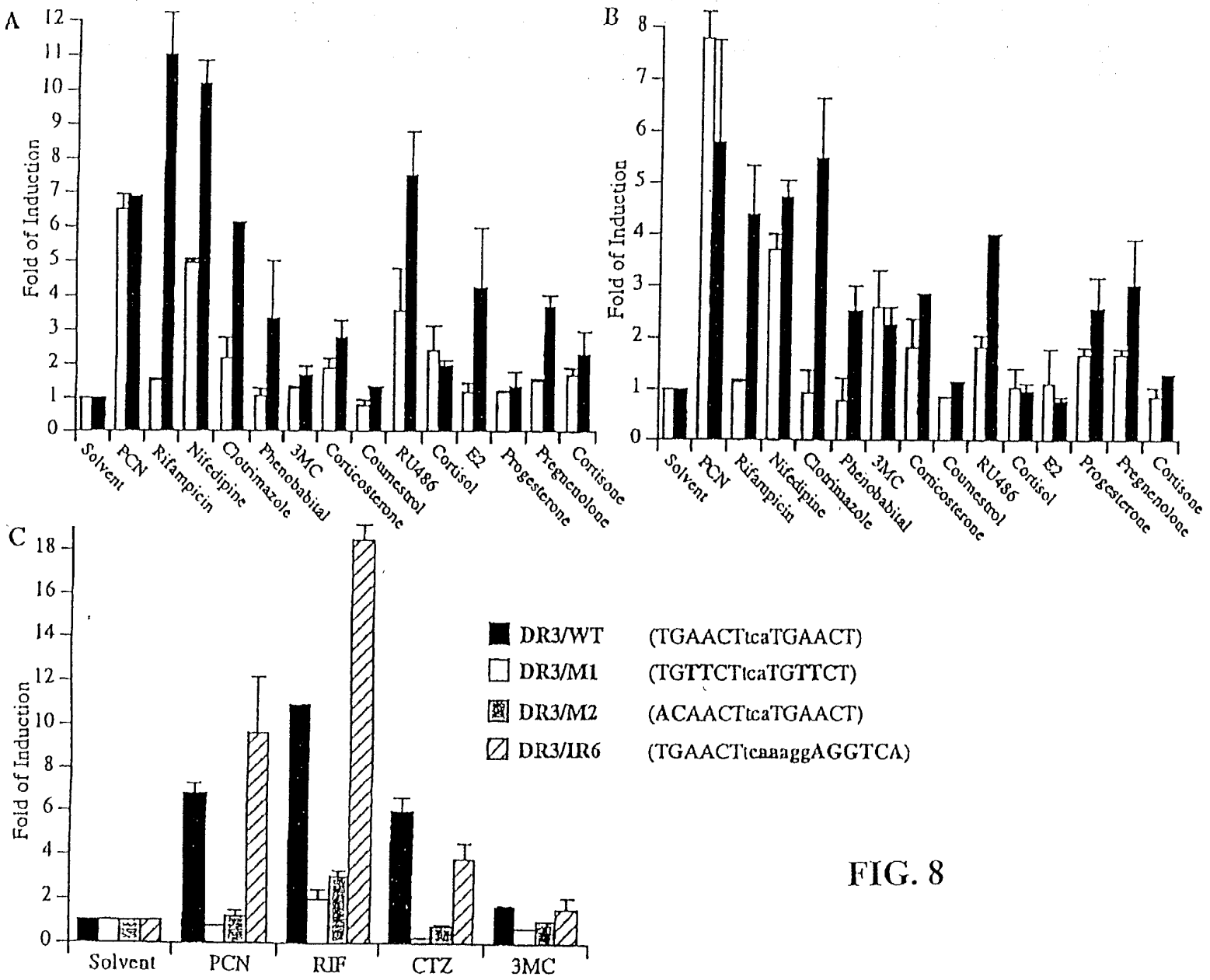
A
Fold of Induction
Solvent
PCN
Rifampicin
Nifedipine
Clotrimazole
Phenobabital
3MC
Corticosterone
Coumestrol
RU486
Cortisol
E2
Progesterone
Pregnenolone
Cortisone
B
Fold of Induction
Solvent
PCN
Rifampicin
Nifedipine
Clotrimazole
Phenobabital
3MC
Corticosterone
Coumestrol
RU486
Cortisol
E2
Progesterone
Pregnenolone
Cortisone
C
Fold of Induction
Solvent
PCN
RIF
CTZ
3MC
DR3/WT (TGAACTtcaTGAACT)
DR3/M1 (TGTTCTtcaTGTTCT)
DR3/M2 (ACAACTtcaTGAACT)
DR3/IR6 (TGAACTtcaaaggAGGTCA)

FIG. 8

EP 0 954 595 B1

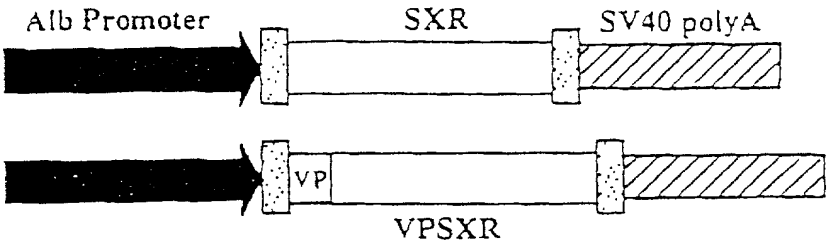

FIG. 9

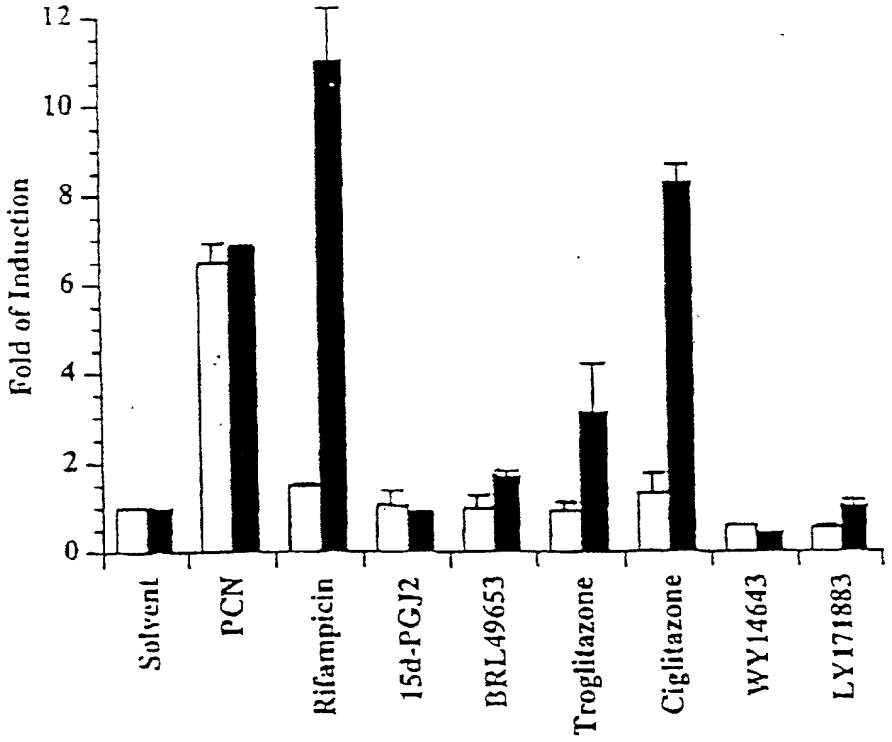

FIG. 10

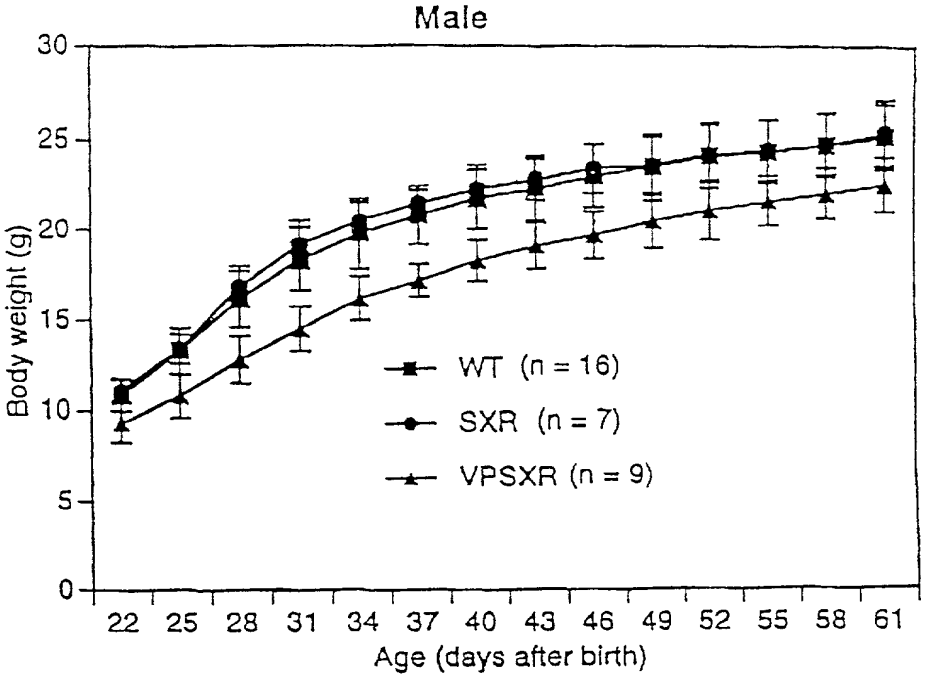
Male
Body weight (g)
30
25
20
15
10
5
0
22 25 28 31 34 37 40 43 46 49 52 55 58 61
Age (days after birth)
WT (n = 16)
SXR (n = 7)
VPSXR (n = 9)

FIG. 11

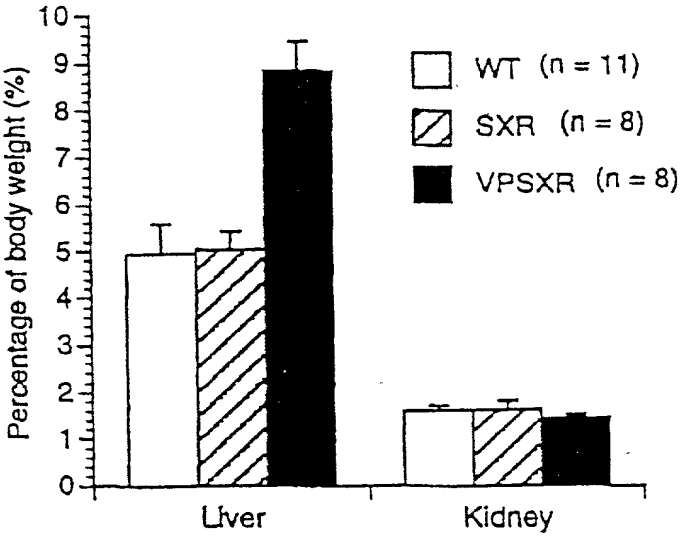
Percentage of body weight (%)
10
9
8
7
6
5
4
3
2
1
0
Liver
Kidney
WT (n = 11)
SXR (n = 8)
VPSXR (n = 8)

FIG. 12